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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,562	06/24/2003	Michael N. Alekshun	PAZ-190RCE	8041

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EXAMINER	
SRIVASTAVA, KAILASH C	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,562	ALEKSHUN ET AL.	
	Examiner	Art Unit	
	Kailash C. Srivastava	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *7-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed 09 March 2009 to Office Action mailed 12 September 2008 is acknowledged and entered.

Informal Matters

2. The information presented in alleged Appendices A and B accompanying the Remarks filed 09 March 2009 is acknowledged, made of record and considered. However, said information should have been clearly marked as Appendix A for the Figures 1-4, and Appendix B for the references presented. As currently presented, Figures 1-4 having the same numbers as those presented on 06/24 and 12/02/2003 are confusing as the new matter.

3. For the record, the List of Claims accompanying response filed 09 March 2009 does not indicate any amended or cancelled claim. Accordingly, the comments presented at Page 8, Lines 6-11 of the REMARKS filed 09 March 2009 are not deemed pertinent.

4. For Applicants' convenience, the Office Action below addresses the rejections in the order that the applicants have argued the rejections in response filed 09 March 2009 to Office Action mailed 12 September 2008; not in the order that the rejections were made in the Office Action mailed 12 September 2008.

Withdrawn Rejections

5. In consideration of Remarks filed 09 March 2009 and to further advance the prosecution of the Claims currently under examination , the following rejections under 35 U.S.C. §112, first paragraph **for recitation of New matter and Lack of written description in the** Office Action mailed 12 September 2008 are herby withdrawn:

- Rejection of Claims 1-6 and 52 for reciting New Matter (i.e., downmodulates at each of Claims 1 and 52, Line 2 or downmodulation at each of Claims 1 and 52, Line 4 and downmodulates at Line 2 in Claims 5-6); and

- Rejection of Claims 1-6 and 52 for lack of written description regarding support for the "prevention".

Claims Status

6. As stated in item 3 *supra*, with the response filed 09 March 2009, an amendment to claims was not filed. Accordingly, the current status of Claims written below is not altered.

- Claims 1-52 are pending;
- Claims 7-51 remain withdrawn; and
- Claims 1-6 and 62 are currently under examination.

Claim Rejections - 35 U.S.C. § 112

First Paragraph Rejection

7. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> ***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

8. Claims 1-6 and 52 are rejected under 35 U.S.C. §112, first paragraph, because the specification, as currently presented does not enable an artisan of skill to "prevent infection of a subject by a microbe by administering to said subject a compound that downmodulates the expression or activity of a microbial transcription factor, wherein said subject is at the risk of developing an infection and said downmodulation of the microbial transcription factor reduces virulence of the microbe such that infection of the subject is prevented". The specification, at the time that the claimed invention was made does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims as currently presented.

From the record of the present written disclosure applicants have merely demonstrated reduction in infection of a microbe in a subject, not "prevention" of the infection in the subject.

Inventions targeted for human "prevention" therapy claiming method(s) of prophylaxis of a certain ailment/infection bear a heavy responsibility to provide supporting evidence because of the unpredictability of the biological responses to therapeutic treatments for prevention. THE STANDARD OF ENABLEMENT IS HIGHER FOR SUCH INVENTIONS because effective prevention or prophylaxis of disease conditions are relatively rare, and may be unbelievable in

the absence of supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to human that would in effect "prevent" the condition/ailment caused by a microbial infection require supporting evidence because of the unpredictability in biological responses to therapeutic treatments or therapeutic prophylaxis. In order to enable the skilled artisan to practice the invention as claimed, applicants would have to demonstrate the functional effect and describe the prophylactic effect, and describe the effective amounts of each ingredient of the composition for the administration of the composition intended for a method of prophylaxis.

Accordingly, undue experimentation without a reasonable expectation of success as to (i) which downmodulator to (ii) which member of (iii) which transcription factor with or without a pharmaceutically acceptable carrier in (iv) which therapeutic amounts would be effective in the instantly claimed (I) method and instantly claimed (II) functional effect of prophylaxis (i.e., prevention) would be required to practice the invention as claimed would be required. This is because of the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as illustrated below.

A. Quantity of Necessary Experimentation

Since the specification does not provide any evidence on how to get prevention of infection from which microorganism infection among those microorganism listed at Page 81, Line 19 to Page 84, Line 6 by which pharmaceutical composition listed at Page 84, Line 10 to Page 89, Line 3 comprising downmodulator for which expression or activity of which microbe according to the plethora of embodiments as candidates according to the list in specification and how much of a solid dose of said composition should be administered to a subject in need thereof to prevent the microbial infection in said subject, an artisan of ordinary skill will have to perform a number of permutations and combinations to obtain a range of dose for the patient population to be administered said composition/compound according to claimed invention. This is because the dosage is a function of at least age/weight among other parameters of a given patient population. Despite the information presented in examples 7 or 9 or 12, the details in currently presented specification do not evidence prevention.

B.Limited Amount of Guidance

As pointed out in item A above, the specification as currently presented despite presenting a plethora of compositions, microorganisms and indications as to what and how a determination may be made, does not provide a clear-cut guidance to obtain the claimed method of preventing a microbial infection" in a subject through administering a particular dosage of a given composition.

C.Limited Number of Working Examples in the Specification

The specification as currently presented best describes the claimed invention in example 7. However, the information presented even in said example also does not show that the claimed downmodulating composition to prevent microbial infection was first administered to the experimental subject followed by a period of time after which said subject was challenged with a certain amount of a microbe in contrast to a control that was not pre administered with a certain dose of the downmodulating composition prior to challenging said subject with a microbe to establish an infection. Furthermore, none of the compounds used in example 4 or 7 is identified. One could not practice the claimed invention with these compounds because what they are has not been disclosed. Thus, the specification as currently presented does not provide any specific example to practice the claimed invention of specifically preventing a microbial infection by administering to a subject a pharmaceutical composition comprising a downmodulatgor as claimed in the instantly claimed invention.

D.Nature of the Invention

As is discussed in items A-C above, the currently presented specification does not delineate the claimed invention by demonstrating that the claimed pharmaceutical composition comprising a downmodulator prevents a microbial infection in a subject.

E.State of the Prior Art

The prior art description in the specification is adequate regarding treating an individual having *a* microbial infection according to the standard clinical practice of administering antibiotics and drawbacks of said method.

F.Relative Skill Level of those in the Art

At least a Bachelor Degree in Biochemical engineering, Biochemistry, Biology, Biomedical Engineering, Environmental engineering, Environmental Science, Microbiology, Molecular biology, or Pharmacology.

G.Predictability or Unpredictability in the Art

Unless supported with illustrative experimental evidence, biological responses are unpredictable. Thus, information obtained under one set of detrimental parameters may not be extrapolated for another set of parameters/environmental or specific conditions.

H.Breadth of the Claims

The claimed invention is drawn upon claims that are not supported by the presently detailed specification.

Claim Rejections – 35 U.S.C. § 112, 2nd Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> ***The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.***

10. Claims 1-6 and 52 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The recitations downmodulates at each of Claims 1 and 52, Line 2 or downmodulation at each of Claims 1 and 52, Line 4 and downmodulates at Line 2 in Claims 5-6 renders said claims confusing, unclear, vague and therefore indefinite because the terms downmodulates or downmodulation have neither been defined in the Claims, nor in the currently presented specification. The Claims as currently presented do not clarify what is meant by the terms downmodulates, or downmodulation? Does it mean inhibition or absence of activity, or that modulation as a whole has been reduced? The metes and bounds for the terms downmodulates, or downmodulation should be clearly defined or alternative terminology used.

All other claims directly or indirectly depend from the rejected claim 1 and are, therefore, also rejected under 35 U.S.C. §112, 2nd paragraph for the reasons set forth above.

Conclusion

11. For the aforementioned reasons, no claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kailash C Srivastava/
Examiner, Art Unit 1657

Kailash C. Srivastava
Patent Examiner
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26 May 2009

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657